

Application No. 10/071,932
Amendment and Response dated June 2, 2005
Reply to Office action of February 8, 2005

Amendments to the Specification

Please replace the paragraph beginning at page 3, line 1, with the following amended paragraph.

The invention provides methods of determining the disease state of a biological specimen based upon a reflectance spectrum residual derived by subtracting from a reflectance spectrum obtained from a test specimen an average reflectance spectrum obtained from a plurality ~~[[i]]~~ of healthy specimens. In a preferred embodiment, members of the plurality of healthy specimens are determined to be healthy based upon the fluorescence spectra emitted by those samples. Typically, the specimen to be tested exhibits a fluorescence spectrum that is not characteristic of healthy tissue.

Please replace the paragraph beginning at page 4, line 5, with the following amended paragraph.

In one embodiment, the plurality of specimens producing the average reflectance spectrum comprises tissue specimens and the test specimen is a tissue specimen of the same type. In one embodiment, the tissue specimens are human cervical tissue specimens, the condition of which is healthy, and the condition of the test specimen is determined by methods of the invention. In one embodiment, cervical tissue producing the average reflectance spectrum are selected from normal squamous tissue, metaplasia, ~~mild~~ mild cervical intraepithelial neoplasia (CIN I), and moderate to severe cervical intraepithelial neoplasia (CIN II/III). In another embodiment, methods of the invention further comprise obtaining additional optical information from the test specimen, and evaluating the additional optical information in comparison to the fluorescence spectrum and the reflectance spectrum from the test specimen to determine the condition of the test specimen. In one embodiment, the additional optical information is video information. In another embodiment, the additional optical information is an optical image.

Please replace the paragraph beginning at page 12, line 14, with the following amended paragraph.

As indicated in step 350, the computer 202 can carry out an analysis using a metric as described in detail at FIG. 7, step 760 below, for example using the Mahalanobis distance as a metric in N-dimensional space. In one embodiment, the test reflectance spectra are truncated to the wavelength regions 391 nm to 484 nm, and 532 nm to 625 nm. In one embodiment, the classifications CIN I and CIN ~~[[II/II]]~~ II/III are the classifications that are possible for a test spectrum that is neither classified as "normal" nor "metaplasia" by fluorescence spectral analysis. As indicated at step 350, the computer 202 classifies the test specimen as having a condition or state of health selected from CIN I and CIN II/III based on the value of the metric computed by the computer 202, provided that the value of the metric does not exceed a pre-determined maximum value.